ASX ANNOUNCEMENT

INITIAL PROOF-OF-CONCEPT RESULTS SHOW INV043 TO BE EFFECTIVE AGAINST MULTIPLE CANCER TYPES

MELBOURNE (AUSTRALIA) 25 May 2021: Invion Limited (ASX: IVX) ("Invion" or the "Company") is pleased to attach the following presentation on the initial proof-of-concept testing results on INV043, the latest Active Pharmaceutical Ingredient ("API") using the Photosoft™ technology.

These proof-of-concept tests were undertaken in collaboration with Invion's research partner, the Hudson Institute of Medical Research (Hudson Institute), on a number of cancer types.

The key findings from the studies are summarised below:

- Promising preliminary results that may have application across a range of cancers
- INV043 has ~50 times greater phototoxicity than Invion's previous API (IVX-P03) and ~600 times greater than Talaporfin sodium (widely used photosensitiser)
- Studies showed INV043 is selectively retained in malignant but not healthy tissues. Furthermore, no toxicity issues were identified up to 50x the therapeutic dose
- Significant regression was observed *in vivo* in T-cell lymphoma, triple negative breast and pancreatic cancer models
- INV043 also displayed fluorescence characteristics under blue light, which illuminated tumour growths

"These results provide direct proof-of-principle for the use of INV043 as a cancer therapy" said Dr Andrew Stephens, Group Head of the Ovarian Cancer Biomarkers Research Group at Hudson Institute. "These early indications are promising, and may lead to new treatment options for some of the most difficult to treat cancers."

Invion's Chairman and Chief Executive Officer, Thian Chew commented: "By using our latest API, these initial proof-of-concept results demonstrate the potential of Photosoft™ technology's applications in cancer treatment. Our next steps include performing further proof-of-concept studies looking at INV043's effect on the immune response as well as exploring its potential to work together with other therapies."

Further details on the studies are included in the attached presentation.

This announcement has been approved by the Board of Invion.

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About Invion

Invion is a life-science company that is leading the global research and development of Photosoft™ technology for the treatment of a range of cancers. Invion holds the Australia and New Zealand license rights to the Photosoft™ technology. Research and clinical trials are funded by the technology licensor, RMW Cho Group Limited, via an R&D services agreement with the Company. Invion is listed on the ASX (ASX: IVX). This announcement was approved for release by Thian Chew, Chairman of the Board. For further information please contact investor@inviongroup.com.

About Photodynamic Therapy (PDT)

Invion is developing Photosoft™ technology as an improved next generation Photodynamic Therapy. PDT uses non-toxic photosensitisers and visible light in combination with oxygen to produce cytotoxic-reactive oxygen that kills malignant cells, shuts down tumours and stimulates the immune system. A potential alternative to surgery, and in contrast to radiotherapy and chemotherapy which are mostly immunosuppressive, PDT causes acute inflammation, expression of heat-shock proteins, and invasion and infiltration of a tumour by leukocytes.

FINDINGS: INITIAL PROOF OF CONCEPT TESTING

May 2021

INVION™

INITIAL PROOF OF CONCEPT: RESULTS AND NEXT STEPS
MULTIPLE CANCER TYPES, THERANOSTIC POTENTIAL

The efficacy of **INV043** against multiple cancer types has been evaluated as part of initial proof-of-concept studies involving *in vitro* and *in vivo* testing, focussed on target indications of clinical need.

ACTIVITY:

- INV043 demonstrated very strong activity against a range of solid tumour types, both *in vitro* and *in vivo*.
- Performance was enhanced >50-fold over Invion's previous API (IVX-P03); and >600-fold over the clinically approved photosensitising agent Talaporfin sodium.

TUMOUR REGRESSION:

- INV043 successfully regressed established T-cell lymphoma, triple negative breast and pancreatic cancers *in vivo*.
- No off-target toxicity was noted.

DUAL THERANOSTIC POTENTIAL:

- **Therapeutic** red light activates the compound, causing rapid cancer cell death and tumour regression.
- **Diagnostic** blue light excites chromophore fluorescence, providing highly visible definition of tumour deposits and margins to the naked eye.

INV043 has high potential as a theranostic agent (combination diagnostic and therapeutic) for use in clinical PDT. Ongoing studies are targeting specific cancer indications with a focus on induced immunity following treatment.

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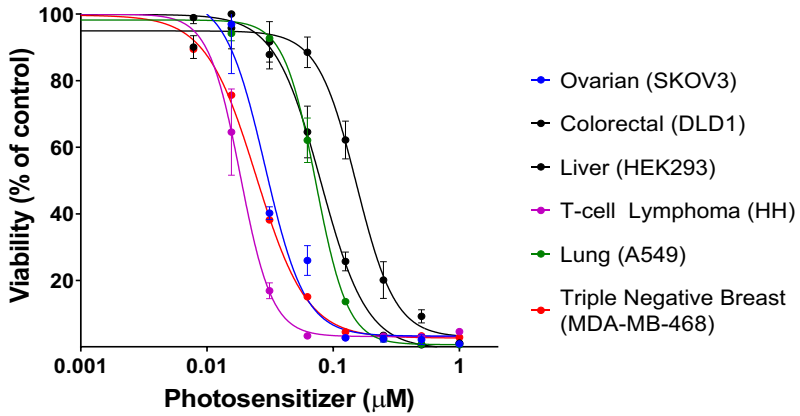
IN VITRO TESTING: DESIRABLE THERAPEUTIC PROFILE
MULTIPLE CANCERS, HIGH POTENCY, LOW NON-SPECIFIC TOXICITY

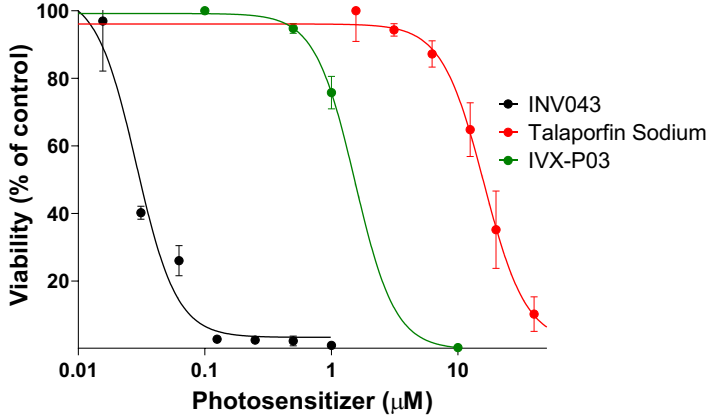
INV043 phototoxicity evaluated in multiple human cancer cell types including ovarian, colorectal, kidney, lung, triple negative breast and T-cell lymphoma. Assays were performed *in vitro* with 4 replicates per data point.

- **INV043 is Active Against Multiple Cancer Types:** with IC90 (the concentration required to kill 90% of cells) as low as 30nM against some cancer types **(Fig 1A)**.
- **Improved Potency:** INV043 had ~50-fold greater phototoxicity than IVX-P03 (previously developed by Invion) and ~600-fold greater phototoxicity than clinically approved photosensitizer Talaporfin sodium **(Fig 1B)**.
- **Low Toxicity:** INV043 was not activated by ambient light, and no evidence of "dark toxicity" was observed until reaching 20-300 times the effective treatment dose **(Fig 1C)**.

A.



B.



C. INV043 Photo- and Dark-Toxicity

Phototoxicity (IC90) μM	Dark Toxicity (IC10) μM	Cancer Type
0.06	9.49	Ovarian (SKOV3)
0.14	29.52	Lung (A549)
0.03	10.25	Lymphoma (HH)
0.20	8.16	Liver (HEK293)
0.33	9.20	Colorectal (DLD-1)
0.07	13.25	Breast (MDA-MB-468)

Figure 1

The research activities involving the use of human tissue samples were carried out in accordance with relevant guidelines and regulations as well as with appropriate Human Research Ethics Committee approval.

IN VIVO PROOF OF CONCEPT: TUMOUR LOCALISATION

SELECTIVE IN PRIMARY AND METASTATIC TUMOURS, NON-TOXIC

Localisation *in vivo* was monitored over time using the intrinsic fluorescence of **INV043** under blue light.

- **INV043 localises to tumour:** Intratumoral (IT - for subcutaneous tumours) or intraperitoneal (IP - for metastatic peritoneal tumours) administration resulted in strong localization to tumour deposits **(Fig 2A-D)**.
- **Selectively retained in tumour tissue:** Both primary and metastatic tumour deposits retained **INV043** for *at least 3 days* following administration **(Fig 2)**. Fluorescence was readily visible under blue light; and highlighted small (<1mm) metastatic deposits that were otherwise invisible to the naked eye **(Fig 2D)**.
- **Non-toxic:** No toxicity was identified over the short (24hr) or long term (1 week) at doses up 5mg/kg; and **INV043** did not induce detectible photosensitivity under ambient light.

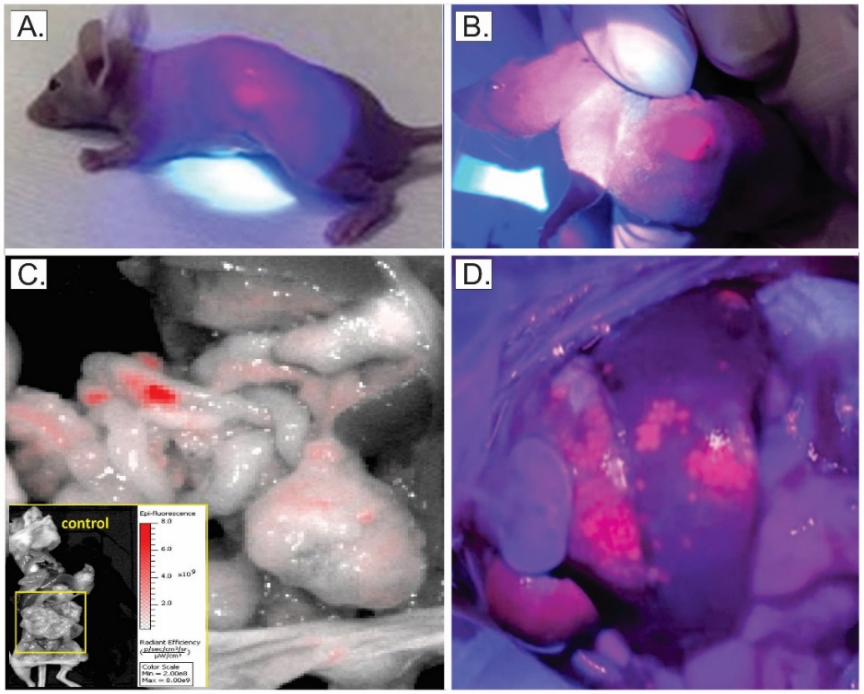


Figure 2. Localization of INV043 in tumour tissue using fluorescence. INV043 was administered at 1mg/kg either intratumorally (IT) or intraperitoneally (IP). Fluroescence was visualized under a blue light and photographed using a standard camera phone (A, B, D) or using an IVIS Lumina III instrument (C). N=4-8 mice/group.

(A, B) INV043 was strongly localized to tumour mass and margins in subcutaneous breast (A) and pancreatic (B) tumours; and within one hour of administration was excluded from surrounding healthy tissues. Fluorescence was retained within tumour mass for at least 3 days.

(C, D) INV043 rapidly localized to metastatic breast (C) and ovarian (D) cancer deposits in the peritoneal cavity after IP administration. Within 24 hours INV043 was not detectible in healthy tissues, but remained concentrated within tumour mass and metastatic nodules throughout peritoneal cavity for at least 3 days. Fluorescence highlighted small metastatic nodules in the peritoneal cavity that were not visible to the naked eye (Fig 2D).

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The research activities involving the use of animals were carried out in accordance with relevant guidelines and regulations as well as with appropriate Animal Ethics Committee approval.

IN VIVO PROOF OF CONCEPT: TUMOUR REGRESSION

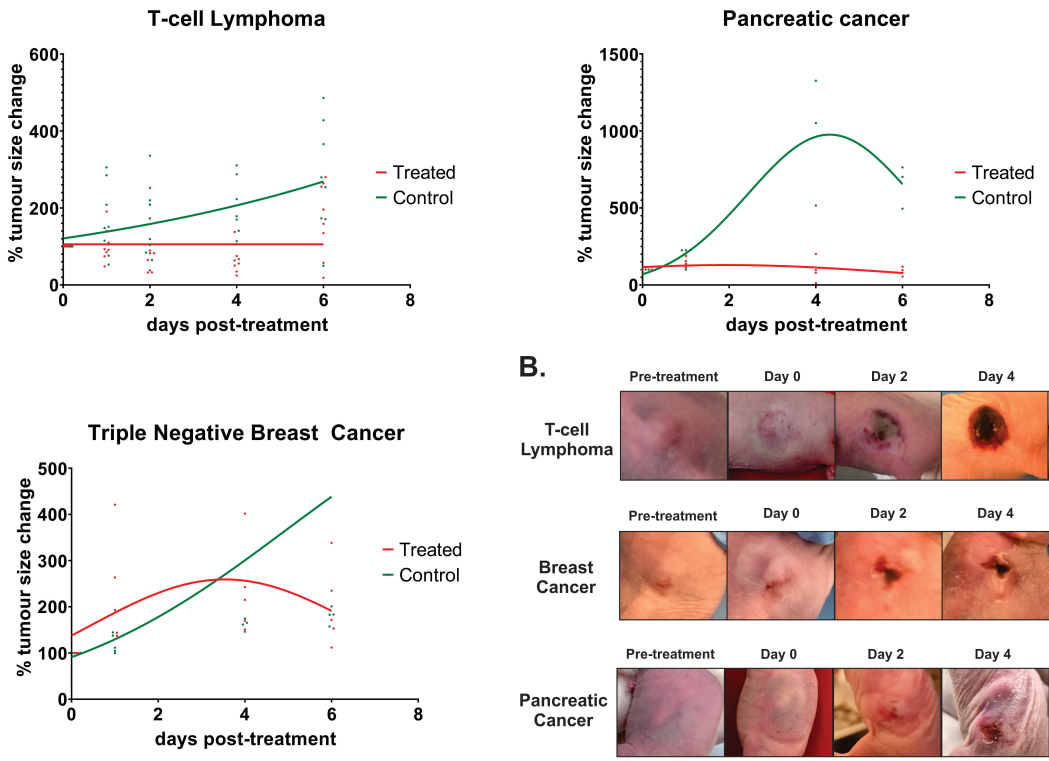
SIGNIFICANT REGRESSION ON MULTIPLE TUMOUR TYPES

INV043 was used to treat implanted T-cell lymphoma, breast and pancreatic cancers *in vivo* (n=4-8/group).

Low dose INV043 (0.1mg/kg) was administered by IT injection and laser light (220J/cm^2) applied after 1.5hrs. Control animals received either laser or **INV043** alone. Tumours were measured for 1 week following treatment to assess change in tumour size.

Significant tumour regression was achieved in all cases.

A.



B.

Figure 3. PDT using INV043 regresses multiple tumour types *in vivo*. T-cell lymphoma, breast or pancreatic cancers grown subcutaneously in nude mice (n=4-8/group) were treated twice within 24hrs as described.

(A) All tumour types regressed following treatment, as determined by decrease in measurable volume. Lymphoma and pancreatic cancers responded within 1-2 days; breast cancers took longer to show evidence of tumour reduction.

(B) Immediately following laser activation tumour tissue became less palpable and developed a "bruised" appearance. Tumour necrosis was evident within 2 days as a distinct darkening of tumour mass beneath the skin. A visible eschar subsequently formed in all cases after 2-4 days. Neither laser nor INV043 without light activation had any measurable effect (*not shown*).

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IN VIVO PROOF OF CONCEPT: TUMOUR REGRESSION

SIGNIFICANT REGRESSION ON MULTIPLE TUMOUR TYPES

Histological evaluation of tumour tissues following **INV043** treatment identified large areas of necrosis in solid tumour deposits **(Fig 4)**, with characteristic nuclear fragmentation and apparent localised neutrophil infiltration. This was consistent with macroscopic pathological observations of substantial necrosis within the tumour and associated hyperplastic regions.

Together the data demonstrate substantial anti-cancer activity *in vivo* of INV043 against three different and typically drug-resistant cancer types.

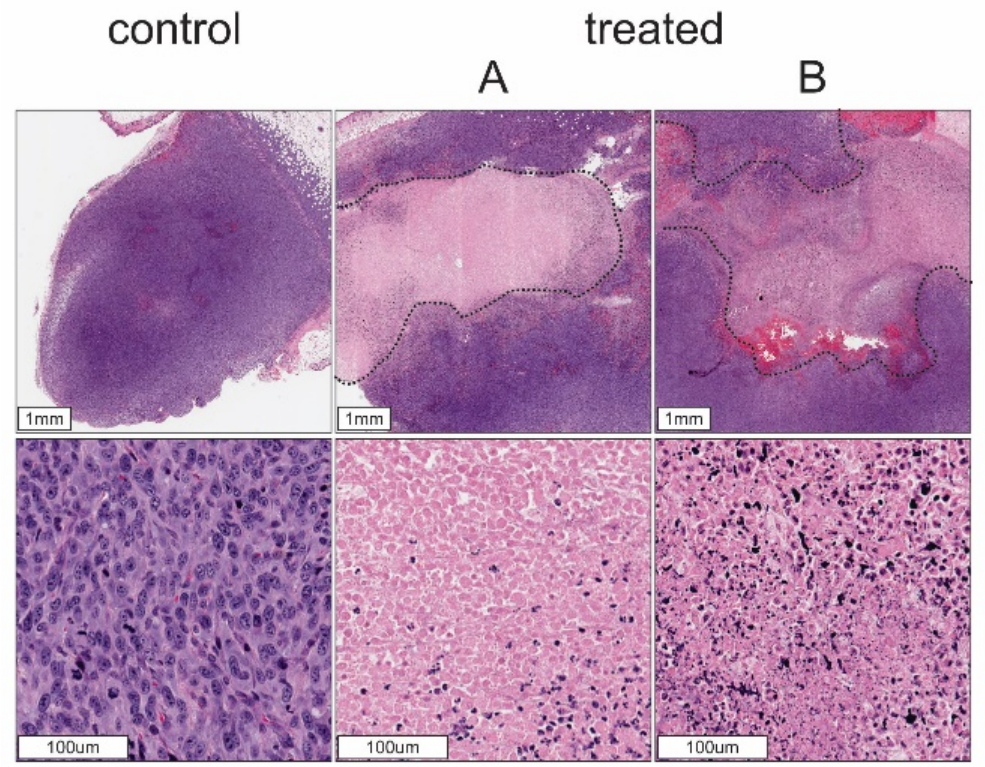

Figure 4. Example H&E staining of breast tumour tissue following PDT using INV043.

Tumour tissue excised 1-week post-treatment was examined by H&E staining. Lower panels are a magnified section of the upper panel; scale is indicated. Untreated control (left) and two treated samples (A, B) right. Nuclear staining appears purple, necrotic tissue appears pink. Treated samples A and B show marked loss of architecture and substantial nuclear fragmentation.

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